NORMATIVE INSTRUCTION (IN) No. 131 OF 30 MARCH 2022

Provides for the Good Manufacturing Practices complementary to sampling activities of raw materials and packaging materials used in the manufacture of medicinal products.

The Collegiate Board of Directors of the Brazilian Health Regulatory Agency, in the use of the attributions vested in it under Article 15, items III and IV, and Article 7, item III of Law no. 9,782 of 26 January 1999, and item VII, paragraphs 1 and 3 of Article 187 of the Internal Regulation approved by Collegiate Board Resolution – RDC no. 585 of 10 December 2021, adopts the following Normative Instruction, as decided upon in the Extraordinary Meeting – RExtra 6, held on 30 March 2022, and I, Director-President, determine its publication.

CHAPTER I

INITIAL PROVISIONS

Section I

Objective

Article 1. This Normative Instruction has the objective of adopting the guidelines on Good Manufacturing Practices for Medicinal Products related to sampling activities of raw materials and packaging materials of the Pharmaceutical Inspection Cooperation Scheme (PIC/S), as complementary requirements to be followed in the manufacturing of medicinal products, in addition to the General Guidelines on Good Manufacturing Practices for Medicinal Products.

Section II

Scope

Article 2. This Normative Instruction applies to companies that carry out operations related to the sampling of raw materials and packaging materials used in the manufacture of medicinal products, including experimental medicines.

CHAPTER II

GENERAL PROVISIONS

Article 3. Sampling is an important operation in which a small fraction of a batch is taken.

Sole paragraph. Decisions on batches of raw materials and packaging materials must be based on trials conducted on representative samples.

CHAPTER III

PERSONNEL

Article 4. The personnel collecting samples must receive initial and regular training in the disciplines relevant to correct sampling, which must include:

I – sampling plans;

II – written sampling procedures;

III – sampling techniques and equipment;

IV – risks of cross contamination;

V – necessary precautions with unstable or sterile substances;

VI – checking the visual appearance of materials, containers, and labels; and

VII – records of unexpected or unusual circumstances.

CHAPTER IV

RAW MATERIALS

Article 5. The identity of a batch of raw materials must be ensured by collecting individual samples from all containers.

Sole paragraph. The identification trials must be carried out on each individual sample.

Article 6. Sampling only a part of the containers is allowed when a qualification procedure of manufacturers and suppliers ensures that no container of raw materials is incorrectly labeled.

Paragraph 1. The qualification provided for in the caption of this article must consider, at least, the following aspects:

I – the nature and status of the qualification of the manufacturer and the supplier of raw materials, and the understanding by these establishments of the Good Manufacturing Practices requirements of the pharmaceutical industry;

II – the quality assurance system of the raw material manufacturer;

III – the manufacturing conditions under which the raw materials are produced and controlled; and

IV – the nature of the raw materials and the medicinal products in which they will be used.

Paragraph 2. Considering the qualification provided for in the caption of this article, the exemption of identification test is possible in each container of raw material received in the following cases:

I – raw materials from a mono-producing plant; or

II – raw materials sourced directly from the manufacturer or in the manufacturer's sealed containers, whenever there is a history of reliability and regular audits are carried out on the

Quality Assurance system of the raw material manufacturer by the medicinal product manufacturer or officially accredited body.

Paragraph 3. It is unlikely that the procedure referred to in the caption of this article can be satisfactorily validated for:

I – raw materials supplied by intermediaries, such as importers, fractionators, and distributors, when the manufacturer is unknown or not audited by the manufacturer of the medicinal product; and

II – raw materials used for parenteral products.

Article 7. The quality of a batch of raw materials may be attested by the collection and laboratory analysis of a representative sample.

Paragraph 1. In the hypothesis provided for in the caption of this article, the samples collected for identity tests may be used.

Paragraph 2. The number of samples taken for the preparation of a representative sample must be determined statistically and specified in a sampling plan.

Paragraph 3. The number of individual samples that can be mixed to form a composite sample must be defined taking into consideration the nature of the material, the knowledge of the supplier, and the homogeneity of the composite sample.

CHAPTER V

PACKAGING MATERIAL

Article 8. The sampling plan for packaging materials must take into consideration at least the following items:

I – the quantity received;

II – the required quality;

III – the nature of the material (for example: primary packaging materials or printed packaging materials);

IV – the production methods; and

V – the knowledge of the packaging material manufacturer's Quality Assurance system based on audits.

Article 9. The number of samples collected must be statistically determined and specified in a sampling plan.

CHAPTER VI

FINAL PROVISIONS

Article 10. Non-compliance with the provisions contained in this Normative Instruction constitutes a health infraction, pursuant to Law no. 6,437 of 20 August 1977, without prejudice to the applicable civil, administrative, and criminal liabilities.

Article 11. Normative Instruction – IN No. 40 of 21 August 2019 is hereby revoked.

Article 12. This Normative Instruction enters into force on 2 May 2022.

ANTONIO BARRA TORRES